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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/713,545	11/15/2000	Russell N. Van Gelder	LBS-002COB	4526
26707	7590	03/10/2004	EXAMINER	
QUARLES & BRADY LLP RENAISSANCE ONE TWO NORTH CENTRAL AVENUE PHOENIX, AZ 85004-2391			LEFFERS JR, GERALD G	
		ART UNIT		PAPER NUMBER
		1636		28
DATE MAILED: 03/10/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)
	09/713,545	VAN GELDER ET AL.
	Examiner	Art Unit
	Gerald G Leffers Jr., PhD	1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 22 September 2003.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 42-54 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 42-54 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. <u>3/4/04</u> |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>9/22/03</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/22/2003 has been entered.

Interview Summary

Attached is an interview summary for a personal interview conducted on 3/4/2004 between the examiner, Dr. James Eberwine and Barbara Luther. The examiner would like to thank Dr. Eberwine and Ms. Luther for proposing the interview.

Response to Amendment

Receipt is acknowledged of a response, filed 9/22/2004, in which additional arguments are presented concerning the rejection of the pending claims as being obvious over the teachings of Kramer et al (U.S. Patent No. 5,112,734) in view of Hartley et al (U.S. Patent No. 5,043,272), and further in view of Ahlquist et al (U.S. Patent No. 5,466,788) or Kwoh et al (PNAS USA, Vol. 86, pages 1173-1177, 1989). The rejection has been withdrawn based upon applicants' arguments and on the basis of the personal interview of 3/4/2004. To summarize, the combination of cited references does not teach a *multi-gene* expression profile of a sample comprising a collection of *linearly amplified specific nucleic acid messages*, wherein said

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amplified specific nucleic acid messages *each* have an abundance which reflects the relative representation of specific nucleic acid messages within the sample [examiner's emphasis added].

Applicants' response of 9/22/04 characterizes the invention as follows:

Based on the fact that mRNA sequences have a poly A end, Van Gelder et al. devised a method to produce a multi-gene profile in which a collection of different nucleic acids therein are in linear proportion to the mRNA species in the sample and therefore maintain the same relative proportion among the synthesized nucleic acid as among the different mRNA species in the sample. The basic method starts with annealing a poly T oligo with T7 promoter to the poly A end which characterizes all mRNA, synthesizing a single cDNA copy of a particular mRNA, and making multiple RNA copies from the cDNA (Fig 1). Because the cDNA are produced in a one-to-one relationship to the mRNA present in the sample, and the cDNA are copied into RNA multiple times, linear amplification occurs. The nucleic acids are produced in numbers which bear a linear relationship to the mRNA present in the sample, and the cDNA are copied into RNA multiple times, linear amplification occurs. The nucleic acids are produced in numbers which bear a linear relationship to the mRNA numbers in the sample. The process simultaneously produces copies of many species of mRNA, in proportion to the number of each mRNA species in the sample. The collection of so-produced nucleic acids thus have the same relative representation as the mRNA in the sample.

This explanation is consistent with the instant specification, which defines linear amplification only in terms of a *population* of target sequences and not with regard to a single target sequence. For example, the specification teaches:

Also, the novel aRNA technology is used to identify sequences of interest from small amounts of nucleic acid by detecting the amplified sequences in the aRNA product. The aRNA amplification is uniform among individual sequences, and thus, it is useful in estimating relative levels of representation of a given sequence relative to other sequences within a population. Such quantitative resolution finds use in molecular diagnostics (such as diagnosing thalassemias characterized by abnormal levels hemoglobin gene expression), where diagnosis can rest not on the absolute presence or absence of a sequence, but on whether a given sequence is present at abnormally high or low levels relative to other sequences. By providing relatively linear amplification, the present invention offers advantages to PCR. (page 16, lines 9-22; examiner's emphasis added)

While the Kramer et al, Miller et al and Kwoh et al references teach a system of initial amplification that is similar to that taught by applicants with regard to formation of a double-stranded nucleic acid comprising an RNA polymerase promoter at one end of the initial double-

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stranded product, Kramer et al and Kwoh et al teach that the initial double-stranded product is formed using a combination of two primers. Miller et al do teach at least one embodiment where a single primer comprising an RNA polymerase promoter is used to generate the initial double-stranded template for subsequent amplification using the cognate RNA polymerase (e.g. see Figure 1). However, neither Kramer et al or Miller et al teach or suggest the use of their methods to amplify *multiple* targets (e.g. multiple pairs of primers known to hybridize to different target sequences, or a single pair of primers that binds to a sequence conserved amongst different target messages) such that *each* amplified message in the expression profile is present in an amount that reflects its relative representation in the original sample. Neither of these references addresses the *relative* abundance of different target sequences in a sample population of such sequences (i.e. an expression profile of a sample). Hartley et al teach the use of pairs of randomized primers to bind to and amplify multiple target sequences, but do not teach the sort of linear amplification of the target sequences that is encompassed by the claims. Rather, Hartley et al teach a logarithmic type of amplification wherein the representation of amplified sequences is dependent upon the ability of all of the target sequences to bind the randomized primers. As stated in applicants' response, "...any set of sample nucleic acids will be amplified in direct proportion to the templates' numbers of binding sites for the random primers." (page 6, 3rd paragraph of the response). Thus, Hartley et al does not teach or suggest the sort of "linear amplification" recited in the instant claims.

The teachings of Kwoh et al are addressed below, but do not offset the deficiencies of Kramer et al and Hartley et al as applied in the withdrawn grounds of rejection (see the new grounds of rejection made below over the teachings of Kwoh et al).

Oath/Declaration

Receipt is acknowledged of a supplemental Oath/Declaration, filed 9/22/2004. It is noted that the examiner did not require the submission of a supplemental oath or declaration. The supplemental oath or declaration is defective, however. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c). The middle initial for James Eberwine has been modified without being initialed (i.e. from James D. Eberwine to James H. Eberwine). This brings into question the correct spelling for Dr. Eberwine's name since the bibliographic data sheet and previous applications all list Dr. Eberwine as James D. Eberwine. It would be remedial to submit a supplemental declaration from Dr. Eberwine with the correct spelling. Applicant is also encouraged to correct the record if necessary.

Information Disclosure Statement

Receipt is acknowledged of an information disclosure statement (IDS) filed 9/22/2004. The signed and initialed PTO Form 1449 has been mailed along with this action.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 42-54 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,291,170 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. **This is a new rejection.**

The claims of the '170 patent are directed to a multi-gene expression profile of a sample comprising a hybridizing target; and a hybridizing probe comprising a collection of amplified specific nucleic acid messages, which amplified specific nucleic acid messages have been amplified *in vitro* simultaneously with RNA polymerase and a single primer linked to a RNA polymerase promoter, wherein the amplified specific nucleic acid messages each have a relative abundance that qualitatively reflects the relative representation of specific nucleic acid messages within the sample. In these claims the collection of amplified specific nucleic acid messages is a probe hybridizing to the target to form a multi-gene expression profile. The amplified specific nucleic acid messages can be aRNA or cDNA. The gene expression profile can be obtain from a single cell, such as a neural cell. The gene expression profile can vary as a function of arousal state, behavior, drug treatment or development.

The instant claims differ from those of the '170 patent in that the do not explicitly state that the gene expression profile is generated by *simultaneous* amplification of the target sequence with a *single* primer/promoter complex. Therefore, the instant claims are broader genus claims that are anticipated by the claims of the '170 patent. Therefore, the claims of the '170 patent necessarily make obvious the instant claims.

Claims 42-54 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 5,891,636. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. **This is a new rejection.**

The claims of the '636 patent are directed to a gene expression library derived from a cell or tissue sample comprising two or more specific nucleic acid messages of various abundances whose levels of representation to other messages within the population reflect the physiological state of the sample, thereby permitting diagnosis of a disease or conditions. The library is prepared by adding a primer complex to a population of messenger RNAs from a cell or cell population where the primer complex comprises a primer sequence complementary and hybridizable to a plurality of the population of mRNAs where the primer complex comprises a promoter sequence in antisense orientation. A double stranded complementary DNA (cDNA) is generated without using a secondary primer and the cDNA subsequently used to linearly transcribe multiple copies of antisense RNAs (aRNAs) that are quantified. Practicing the methods of the '636 patent would necessarily generate a gene expression profile where the relative abundance of the amplified sequences would reflect the relative representation of the different target sequences in the cell or cell populations. Two or more amplified sequences can be detected by hybridization techniques, such as northern or Southern hybridization. The sample can be derived from blood, brain, bone, heart and other cell types. The primer complex can consist essentially of poly(dT).

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The instant claims differ from those of the '636 patent in that they do not explicitly state that the gene expression profile is generated by amplification of the target sequence with a primer/promoter complex that binds a plurality of target sequences and where the template cDNA is not generated with a second primer. Therefore, the instant claims are broader genus claims that are anticipated by the claims of the '636 patent. Therefore, the claims of the '636 patent necessarily make obvious the instant claims.

Claims 42-54 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4-6, 10 of U.S. Patent No. 5,545,522. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. **This is a new rejection.**

The claims of the '522 patent are directed to a process for amplifying at least one nucleic acid sequence using a single species of primer complex, the process consisting essentially of synthesizing a first nucleic acid by hybridizing the primer complex to the target sequence and extending the primer complex to form a first strand complementary to the target sequence and synthesizing a second strand complementary to the first strand, where synthesis of the second strand is primed by a 3' loop of the first strand, and subsequently transcribing copies of RNA initiated from the promoter region of the primer complex. The methods of the '522 patent can be practiced with a primer/promoter complex that binds the poly(A) tail of mRNA from eukaryotic cells. Synthesis of the first strand can occur *in situ*, within a single cell. The amplified RNA can be detected by hybridization to a labeled polynucleotide probe.

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The instant claims differ from the cited claims of the '522 patent in that they do not explicitly state that the gene expression profile is generated by *simultaneous* amplification of the target sequence with a *single* primer/promoter complex. In embodiments encompassed by the claims of the '522 patent where multiple target sequences are amplified, a multi-gene expression profile would necessarily be generated where the amplified products would have necessarily been linearly amplified such that each amplified product would reflect the relative representation of the amplified target sequences in the original reaction sample. Therefore, with regard to the basic method of linear amplification of a plurality of target sequences in a sample, the instant claims are broader genus claims that are anticipated by the claims of the '522 patent. Therefore, the claims of the '522 patent necessarily make obvious the instant claims.

With regard to limitations regarding hybridization on a northern or Southern blot, and particular cell types, it would have been *prima facie* obvious to use techniques of hybridization and cell types well known in the art at the time of the invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a new rejection.

Each of the rejected claims is directed to a multi-gene expression profile of a sample comprising a collection of linearly amplified specific nucleic acid messages, wherein said amplified specific nucleic acid messages each have an abundance which reflects the relative representation of specific nucleic acid messages within the sample. The rejected claims encompass embodiments where multiple primer/promoter sets are used to amplify the different target sequences within the sample.

The specification solely talks about generation of an expression profile for a sample where each amplified sequence is in an abundance that reflects the relative representation of a specific target sequence in the sample where a single primer linked to an RNA polymerase promoter is used to simultaneously amplify the different target sequences corresponding to the different genes in the profile. For example, the specification exemplifies an embodiment where an oligo-dT/T7 RNA polymerase promoter is used to direct linear amplification of multiple RNA species within a sample in a single reaction (e.g. Figure 1). Alternatively, the specification describes an embodiment featuring a T7 promoter primer comprising a sequence complementary to sequences found in messages for a family of G-coupled protein receptors to amplify a group of related, but different messages from a sample in a linear fashion (e.g. page 26, last paragraph). Nowhere does the specification address the use of, for example, multiple and different primers to generate a gene expression profile of a sample where each amplified sequence is in an abundance that reflects the relative abundance of the target sequence in the original sample. Therefore, the broad scope encompassed by the instant claims is impermissible NEW MATTER. Applicants

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are invited to indicate those sections of the instant specification that would necessarily provide support for the use of multiple primer/promoter complexes in the methods of the rejected claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 43 and 53-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection.**

The metes and bounds of the phrase "...amplified simultaneously with RNA polymerase and primer linked to RNA polymerase promoter..." are unclear. It is unclear, as the phrase is currently written, whether the RNA polymerase and the primer are linked to an RNA polymerase promoter. Further, the absence of an article before the words "primer" and "RNA polymerase promoter" make it unclear whether a single or multiple primers and/or promoters are being claimed. It would be remedial to amend the claim language to include the appropriate articles.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 42-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kwoh et al (PNAS USA, Vol. 86, pages 1173-1177, 1989). **This is a new rejection.**

Kwoh et al teach the construction and use of a transcription-based amplification system (TAS) that can be used to amplify a given target sequence from within a population of sequences (e.g. Figure 1). In the system taught by Kwoh et al a pair of specific primers are used to generate a cDNA product from a low abundance messenger, where the cDNA comprises an RNA polymerase promoter that can drive transcription of the target sequence (e.g. Figure 1, cDNA synthesis I/RNA transcription I). Kwoh et al teach that their system allows the amplification of a target sequence from one HIV-infected CEM cell (a human lymphocyte cell) in a population of 10^6 uninfected cells (e.g. Abstract; Figure 4). Kwoh et al teach the detection and quantification of their amplified target sequence (both cDNA and RNA) when immobilized on a nylon membrane (e.g. Figure 2). Kwoh et al further teach a bead-based sandwich hybridization assay utilizing the amplified product (e.g. Abstract; Table 1). Kwoh et al specifically contemplate and suggest the use of their system to determine the abundance of a particular transcript over time

during the clinical stages of disease and/or before and after treatment (e.g. HIV in different clinical stages of the disease).

Kwoh et al teach an RNA promoter-based amplification system that is analogous to that taught by applicants, except that it features the use of two primers that are specific for a single target sequence. Kwoh et al do not explicitly teach the use of a control target sequence as a reference for comparison of the levels of their target sequence (e.g. a portion of the HIV genome) in their sample.

The use of an “internal” standard where primers directed to a second, control sequence within the sample would allow the skilled artisan to utilize the amplified control sequence as a reference for the standardization of the amplified target sequence (e.g. HIV) from samples taken under different conditions (e.g. isolates from the different clinical stages of HIV infection). Such “internal” standards are and were known in the art (e.g. ribosomal RNAs in a sample for northern blot analysis of different samples; see the teachings of WO 88/10315 below).

It would have been obvious to one of ordinary skill in the art at the time of applicants’ invention to modify the teachings of Kwoh et al to include the use of a control target sequence such that a reference amount of amplification product would be present for reference to, and standardization of, the amplified target sequence because Kwoh et al teach that it is within the skill of the art to use their methodology to determine the abundance of a particular target sequence under different conditions (e.g. different clinical stages of a disease). One would have been motivated to do so in order to receive the expected benefit of providing a reference against which the level of amplified target sequence in the sample could be standardized. Absent any evidence to the contrary, there would have been a reasonable expectation of success in practicing

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the methodology taught by Kwoh et al for determining the level of a target sequence in different samples under different conditions with a control target sequence so as to provide a standardization reference for amplification of the desired sequence. The use of such an “internal” standard would necessarily generate a *multi-gene* expression profile where the amplification of *each* of the amplified sequences is linear in the sense meant by applicants and reflects the *relative abundance* of each target sequence (e.g. HIV and the control sequence) in the sample.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to utilize any type of host cell known in the art which had already been used for characterization of gene expression levels (e.g. with northern blot analysis and/or PCR).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 42-54 are rejected under 35 U.S.C. 102(a) as being anticipated by Gingeras et al (applicants’ submission, WO 88/10315; see the entire application). **This is a new rejection.**

The Gingeras et al application teaches the TAS system for transcription-based nucleic acid amplification/detection of target sequences taught by the Kwoh et al reference of record and described above (e.g. see Figure 1 and the Summary of the Invention for the application; Gingeras and Kwoh are both authors on the Kwoh et al reference). The Gingeras et al

application further teaches the use of an “internal” standard wherein a control template (e.g. a sequence encoding B-globin) is kept at constant levels in the reaction sample so that there is a reference sample for quantification of the test sequence (e.g. HIV; see Example XI on pages 52-53; also page 11, 2nd paragraph and Figure 3). In Example 11, where two target sequences are amplified simultaneously using two sets of primers, each set of primers specific for one of the two target sequences, a gene expression profile is generated that provides a measure of the relative abundance of each of the target sequences in the original sample. Since the amplification is not logarithmic, featuring the same RNA polymerase amplification approach taught by applicants, the amplification is linear with respect to both sequences. Thus, Gingeras teaches each of the claim limitations. It is understood from reading the Gingeras et al reference that the methods are intended to address the problems with traditional PCR amplification techniques known in the art and are not limited to any particular type of cell.

Conclusion

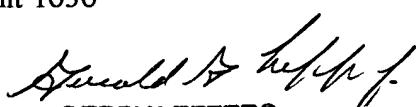
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gerald G Leffers Jr., PhD
Primary Examiner
Art Unit 1636

ggl



GERRY LEFFERS
PRIMARY EXAMINER